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ABSTRACT

Software designed to promote the use of open-ended investigations in science education was evaluated in a study of whether using case-based simulation enhances students' understanding of ethical issues and data interpretation in science. The software was a DNA gel electrophoresis simulation that enabled students to conduct simulated genetic tests. Students chose a case with a genetic disease, researched the disease, and presented their test results. Forty-three college students, mostly nonscience majors, participated in the study. To evaluate the impact of the case-based simulations, an interdisciplinary team designed and administered qualitative and quantitative measures assessing students' interest, confidence, understanding of ethical issues, and interpretation of data. Students' understanding of ethical issues associated with genetic testing increased significantly for men in the experimental group. The case-based simulation enhanced interest in biology and confidence in understanding biology, particularly for female students. Four appendixes contain a case example, the student survey of interest and confidence, a case analysis task, and the scoring rubric for the task. (Contains 3 figures and 25 references.) (SLD)

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ED 431 807

Increasing Interest, Confidence and Understanding of Ethical Issues in Science through Case-Based Instructional Technology

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ABSTRACT

Open-ended computer simulations enable students to solve scientific problems through case studies in areas such as human genetics, infectious diseases, forensics and ecology. The software we evaluated was designed to promote the use of open-ended investigative simulations in science education and is a DNA gel electrophoresis simulation that enables users to conduct restriction analyses and Southern blots of the DNA sequences. Students chose a case with a genetic disease (e.g., breast cancer), ran genetic tests using the electrophoresis simulation, researched the disease and presented their results both at an electronic and a live poster session. Class testing was conducted within a university introductory biology course and focused on three questions:

Does using the case-based simulation enhance students' understanding of ethical issues and/or data interpretation in science?

Does the simulation influence students' confidence in understanding biological concepts?

Does using the case-based simulation affect students' interest?

To evaluate the impact of case-based simulations we formed an interdisciplinary team to design, administer and analyze qualitative and quantitative measures assessing students' interest, confidence, understanding of ethical issues and interpretation of data. Students' understanding of ethical issues associated with genetic testing increased significantly for those in the experimental group. Students' understanding of data interpretation increased significantly for men in the experimental group. The case-based simulation enhanced interest in biology and confidence in understanding biology, particularly for female students.

Many beginning students have a great deal of difficulty envisioning events of molecular metabolism and fail to see how these events impact their everyday lives. Given the increasing social and ethical implications of DNA research in biotechnology, medicine and genetic engineering, it is important for students to develop some understanding in this area and connect this knowledge later on to future situations in their lives.

Case-based learning may be an effective way to engage students in learning these principles, since it encourages problem-motivated investigations of biological phenomena (Stepien & Gallagher, 1993), especially, if students first grapple with problem-based cases and then build on the ideas presented in the cases by generating projects (CTGV, 1997). A case-based orientation to computer simulations involves students in problem posing, problem solving and peer persuasion (Peterson & Jungck, 1988; Stewart, Hafner, Johnson & Finkel, 1992).

There are some powerful symbolic computer simulations developed to promote learning of classical genetics, in which students use, elaborate and revise explanatory models such as Jungck & Calley's (1985) GENETICS CONSTRUCTION KIT and CATLAB (Kinnear, 1982). Previous research investigating the learning resulting from these simulations has used protocol analysis of individual subjects thinking aloud to a researcher as they solved genetics problems (Simmons & Lunetta, 1993; Stewart, Hafner, Johnson & Finkel, 1992) and has provided composites of successful problem solving behaviors. One of the primary goals of problem-based case pedagogy is to foster problem solving skills in students through exposure to real life problems or dilemmas (Barrows, 1998; Lundeberg, 1999). Listening to students solve problems aloud has provided a window into the inquiry process in many fields, including law (Lundeberg, 1985), and biology (Lundeberg, Shearer, Bergland, Klyczek & Mogen, 1998, In their analysis of the conversations of pairs of students as they worked through an open-ended

case-based simulation, Lundeberg, Shearer, Bergland, Klyczek & Mogen, 1998 found that shoed students engaged in peer collaboration and metacognition (reflecting on their thinking) along with scientific inquiry.

While these process studies have provided insight into the scientific thinking processes students use to solve case-based problems, they have not provided evidence that students' understanding has been enhanced. Thus, a major focus on our research was to assess the outcome of whether using this case-based simulation increased students' understanding of biology. In some studies of problem-based learning in the sciences, achievement has been measured by standardized examinations (e.g., Norman & Schmidt, 1992). Even though students' knowledge of facts is not increased as assessed on traditional tests, problem-based learning may encourage ways of thinking or scientific understanding not measured with traditional assessments. Rather than use traditional multiple-choice tests, we used a case-analysis task to assess changes in students' understanding of ethical issues and data interpretation.

In addition to assessing understanding, we also evaluated whether the simulation influenced students' confidence in understanding biological concepts. Confidence in understanding is a form of metacognition, that is thinking about one's thinking. Self-assessment of knowledge is a primary component in academic learning. If students do not feel confident in their understanding of a concept, they can devote more time to learning the concept; if they are confident in their knowledge, they can attend to more difficult concepts. Previous research on confidence has shown that judgments of knowing accurately predicted subjects' recall retention (Leonesio & Nelson, 1990). Thus, confidence in understanding was measured using judgments-of-knowing measures in which we asked students to estimate their knowledge of biological concepts.

Finally, introductory biology is a required course for many university students and may not be intrinsically interesting, or viewed as relevant to students' lives. Many women, in particular, lose interest in science (Kahle, 1999). Relating science to problems people encounter in their lives may encourage more female interest in science (Smist & Barkman, 199?). Therefore, we also assessed whether case-based learning increased interest in science.

METHOD

Context of the Study

This study was conducted within the context of an undergraduate introductory biology course in a comprehensive Midwestern university. This course included laboratory sections based on lectures students received. The evaluation of this case-based simulation occurred near the end of the semester, after students had listened to lectures on genetics (the information reinforced in this simulation).

Participants

Most of the students were non-science majors, enrolled in the second semester of college at this primarily Caucasian university. Over three nights 43 students (15 men and 24 women) from Biology 100 (75% of the class) volunteered to participate in this case-based simulation for extra credit. Twenty-five percent (14 students: 6 men and 8 women) chose not to participate. There were no significant differences in students' grades in biology 100 between the experimental group (volunteers) and the control group (those who chose not to volunteer). [1]

[1] While random assignment of control versus experimental groups would have been preferable from a research perspective, it was not practical from a classroom perspective.

Description of Case It! Project

Case It! Is a National Science Foundation-sponsored project to integrate molecular biology computer simulations into a framework for case-based learning for introductory biology students worldwide. Students use investigative simulation tools to study problems in human genetics, forensice, phylogeny, politics, and other disciplines and then defend their results using the 3-P's approach of the BioQUEST Curriculum Consortium: problem-posing, problem-solving, and peer persuasion (Peterson & Jungch, 1988). Two of the authors developed a DNA gel electrophoresis/Southern blot simulation to analyze any DNA sequence using any combination of restriction enzymes and probes (Klyczek and Bergland, 1996; Bergland, 1997; Bergland and Klyczek, 1998). They obtained DNA sequences for genetic disease conditions from Internet data banks, and developed hypothetical case scenarios for families being tested for these conditions.[2] An example of Case 5: Breast Cancer Susceptibility is provided in Appendix A.

The DNA Electrophoresis module used in this study runs realistic gels and Southern blots of the resulting DNA fragments. Electrophoresis is a research technique used by molecular geneticists to move negatively charged DNA molecules in an electric field. The DNA will migrate to the positive pole of the field, moving at different rates: the smaller fragments move more quickly and separate themselves from the larger ones. The use of a Southern blot will highlight the genetic fragments of interest. An example of the results from a Southern blot is illustrated in Figure 1

--Insert Figure 1 about here—

[2] Software modules described in this paper can be downloaded at no cost to educators for the Case It! Web site (http://www.uwrf.edu/caseit/caseit.html) for both the Macintosh and Windows 95 operating systems. Persons interested in becoming involved in the project should contact mark.s.bergland@uwrf.edu for details.

Figure 1 shows a Southern blot for the sickle-cell anemia case. Both parents (lanes 2 and 4) are carriers of the sickle-cell gene, and passed this gene to their unborn fetus (lane 3) but not to their unaffected daughter (lane 1).

Description of student task

Working with a partner, students using the software chose one of the cases from human genetics (sickle-cell anemia, Huntington's disease, Alzheimer's disease, cystic fibrosis, Duchenne's muscular dystrophy, Phenylketonuria, and breast cancer) to study. Students first played the role of genetics lab technicians, going through the procedures involved in DNA testing for genetic diseases (e.g., obtaining DNA sequences, loading these DNA fragments into wells). This is primarily what students accomplished during their first interaction with the software. On their own, in later sessions at the computer lab, students conducted tests on at least three of the case variations in the disease they selected, and saved images such as those in Figure 1 to place on web-page "posters" for discussion via bulletin board accessed from the Case It! Web site (http:www.uwrf.edu/caseit/caseit.html). After they conducted the tests and used the Internet to search for additional information on their disease, they presented their posters electronically on the Internet. Figure 2 is a portion of an actual student webpage poster in which the implications of Alzheimer's disease are communicated to

--Insert Figure 2 about here—

"family members." This gave students an opportunity to ask questions regarding one another's posters and to revise their posters prior to the live poster conference. During the live poster conference, students were put in the role of genetics counselors and asked to consider ethical consequences when they interpreted results from the human genetics cases. Faculty members played the role of family members involved in genetics counseling who were hearing the results of their DNA tests.

Procedure

We assessed confidence, interest and understanding after students studied DNA structure, gene function and classical genetics, and administered these instruments a second time, seven weeks later, after students completed their case-based research. We administered the following measures:

1) pre and post questionnaires designed to assess students' interest and confidence; (included in Appendix B)
2) a case analysis task designed to measure students' understanding of scientific concepts and ethical issues before and after the simulation, and
3) open-ended evaluations from all students asking them to "give your general impression of the Case It class project."

The case analysis task included a case about a couple who are expecting their third child and suspect that their oldest child may have Fragile X Syndrome, so they undergo genetic counseling (see Appendix C for the complete case). The case presented background on this disease and results from gel electrophoresis and Southern blots of the DNA fragments. Students interpreted the results and answered these questions:

"As a genetics counselor, what would you advise this family about ethical issues raised by these results?," and

"Based on your understanding of the molecular basis of the mutation, explain why the fragments in lanes 6, 7, and 8 are in different positions."

In addition to the above assessments, six preservice science teachers interviewed biology students at the live poster sessions and analyzed students' electronic conversations.

Data analysis

Categories of analysis for the responses to the open-ended questions and the transcripts of interviews were constructed by following Strauss and Corbin's (1990)

approach to grounded theory generation. Raters searched the data for dimensions, sorted the data and collapsed and realigned dimensions until there was consensus between raters and no new categories emerged. An interdisciplinary team consisting of a biologist, educational psychologist and six preservice science teachers devised a scoring rubric to use with the case analysis task after reading 12 answers as a group and coming to consensus on how these should be rated. These raters were blind as to whether students' answers on the case analysis task were pre or post. A pair of two raters jointly scored both open-ended questions on the case analysis task. Appendix D contains the scoring rubric we used to analyze student responses to these questions.

RESULTS

Influence on understanding ethical issues and interpreting scientific data

Students were asked to put themselves in the role of a genetics counselor and to describe any ethical issues associated with the results of this case. Using a repeated measures ANOVA we found a significant within subjects effect, $F\ (1,53) = 3.45$, $p < .06$. Students' understanding of ethical issues increased significantly for those in the experimental group, $t = 2.24$, $p < .03$, but not for those in the control group, $t < 1$. These changes are illustrated in Figure 1.

Insert Figure 3 about here

After students analyzed the case concerning the Fragile X Syndrome, they were asked to explain why fragments on the gel blot were in different positions. This allowed us to assess if they understood the process of electrophoresis and if they could interpret gel blots. Using a repeated measures ANOVA we found a significant interaction between sex and experimental condition, $F\ (1,53) = 4.17$, $p < .05$. Men in the experimental group significantly increased their understanding between the pre and the post case analysis

task, $t = 2.97$, $p < .01$, whereas pre and post test differences for the other groups were non-significant.

During interviews held during the poster sessions, and in their open ended comments 95% of the students reported gaining greater understanding of one or more of these aspects of biology: DNA and human genetics, genetic testing, knowledge of particular diseases, and/or application of biology to their future lives. Of those who reported learning more, 35% reported gaining greater understanding of DNA and human genetics as this quote illustrates:

"I think this was a really valuable project because it taught me a lot about DNA, blotting and how to determine the differences between the mutated gene and the normal one."

Twenty-eight (28)% made comments related to understanding more about the processes of genetic testing, for example:

"I learned a lot about DNA and genetic testing. I think it's a good thing to be aware of the prenatal testing opportunities available, should I ever want to take advantage of DNA testing when I decide to have children."

Finally, thirty-one (31)% gained knowledge of particular diseases as these quotes illustrates:

"I didn't know about PKO until I chose the disease. I am glad I did."

"I thought that the live poster session was a good experience because we had to really get to know the disease because we didn't know what was going to be asked."

Twenty (20) percent of the students reported that they gained an understanding of biology that was relevant to their future lives, as these comments illustrate:

"I learned TONS of things on Breast Cancer something that I might need to use in the future. "

"I think that the Case It! project overall was a valuable because it made me relate this to my actual life. It wasn't just an experiment."

"Being a non-biology major I learned a lot. This is what I will carry with me from this class."

During interviews, students reported that questions from other students prompted teams to do additional research, for example Nina and Stacy acknowledged., " ... some people did ask good questions that we didn't know and so we had to do some more investigating and stuff." We examined the Internet conversations along with their initial and final posters of these two women. Nina and Stacy made three changes to their electronic poster on cystic fibrosis due to questions from peers. One was a stylistic change, but the other two changes involved additional research and adding information. In response to a student who asked a question regarding the diet restrictions of persons with CF; Nina wrote, "I really don't know if CF patients have a restricted diet. I know that they are lacking several digestive enzymes that help with absorption. I'll have to get back to you on that and add it to our poster! Thank you for bringing it up!" This team later added a paragraph to their poster regarding suggestions for diet. The second change involved clarifying information on their poster and, in the process, correcting an initial misunderstanding. Nina and Stacy were asked this question during the Internet conference:

"I only have one small question for you that you would possibly want to explain on your poster; when you mentioned this makes men infertile. Is this for life, and what is the percentage of this happening for these men. I would think this would obviously be a concern to people finding out this information."

One member of the team responded, "Thanks for the comments...CF does unfortunately make ALL men infertile for life. I'm not exactly sure what goes wrong in the reproductive

tract. I'm going to try and see if I can find some more background on it though. I'll post a new message regarding that when I have a more in depth answer for you as well as add it to the poster."

Two days later the other team member corrected her partner, writing: "Okay, we have a small correction, 98% of males are infertile due to CF. In most males the vas deferens is blocked by the mucus secretion or they can be abnormally developed before birth. In this 98% of males the infertility is irreversible and in the remaining 2% sometimes the vas deferens isn't completely blocked and some healthy sperm can get through, however, a sperm count will want to be used to confirm."

Communicating with peers over the Internet seemed to push students into deeper understanding and may have contributed to students' confidence in understanding, as illustrated by the comments reported in the next section.

Influence on confidence in understanding scientific concepts and procedures

Before and after the simulation, students rated their understanding of methods for detecting genetic diseases involving DNA, DNA electrophoresis, interpretation of results from genetic tests, reasons for doing genetic testing , ethical issues involved in human genetics testing, and ability to locate current resources on diseases. In assessing their confidence students used a scale typical of those used in confidence research, rating their confidence in understanding from 1 (no confidence) to 5 (very confident0 (e.g., Lundeberg, Fox, & Punchochar, 1994). Analysis of variance showed significant effects for experimental condition, F (1,49) = 12, $p < .001$. Followup t-tests showed that the experimental students' self-assessments of confidence in their understanding of the above areas increased significantly, t =7.19, p <.0001. Moreover, women in the experimental group gained greater confidence on the post-assessment (mean = 4.35; s.d. = .40) than did men (mean = 4.08; s.d. = .27) , t = 2.45, p <.01. Students' comments confirmed these gains

in confidence and provided some insight into students' reasons for increased confidence. For example, the value of interpreting results from gels was appreciated by several students, as this quote illustrates:

" The outcome (of the computer simulation) was very worthwhile because I actually ran the gel and had to interpret it on my own without a professor to confirm or deny my findings."

Numerous students liked being able to correct errors easily:

"The computer simulation was very informative and you didn't have to worry about mixing things up because you could just start over. I think it helped me remember steps easier for the test."

Several students commented on the value of communicating with peers though Internet conferencing, as these comments illustrate:

"Through the use of the conferencing session we were able to expand and enhance our poster."

"The Internet conferencing was helpful because we got told how we could have improved our poster instead of just making a poster and handing it in."

"It seemed that you learn when you are faced with answering questions from others."

Finally, several students commented on the value of learning communication skills in the context of role-playing a genetics counselor, e.g.,:

"I think it helped the students interact with each other. Also, this gave us an important insight on what a genetic counseling job is like.

"I thought that this was a very valuable opportunity. It gave us as students a chance to experience first hand the difficulties that come with DNA testing. It was also good because it taught us discussion skills because we had to tell the family what was going on."

"I can't speak for anyone else, but I liked being a genetic counselor. It gave me order, direction and focus."

In the Internet conferencing, students probed for information regarding ethical issues that a genetics counselor might face. For example, in responding to a poster on Alzheimer's disease, a student asked, "What would you do if a loved one had the disease? Since the disease develops over time would you look at assisted suicide? How close are they to having a cure?" The student team responded, "Yes, I will agree it would be very difficult to find out that a loved one had Alzheimer's. The best thing that I could honestly do would be to support them and to give them all of the love and care that you possibly could. No, I would not look at assisted suicide for a patient with Alzheimer's disease, this disease comes on gradually and does not affect the person all of the time...I don't think that it is worth ending someone's life for this..."

Influence on students' interest

Before and after the simulation, students rated their interest in DNA Electrophoresis and human genetics. Analysis of variance showed significant effects for sex, F (1,49) = 4.04, $p < .05$. Followup t-tests showed significant gender differences on the post-survey, $t = 3.34$, $p < .003$, with interest for women (mean = 4.1; s.d. = .56) rated higher than that of men (mean = 3.4; s.d. = .67) in the experimental group. During the interviews and open-ended responses, students reported finding the case-based simulation relevant, and enjoying the simulation case activities, although many found the process of analyzing data, doing research, constructing a poster and participating in the electronic and live poster sessions to be a lot of work.

"It is my opinion that the Case It! project was a very fun and interesting means to learn more about genetic disorders and how they affect human lives."

"It made all the information on DNA seem purposeful."

"I thought the Internet conferencing was the most fun. It was really interesting to answer the questions from the other students and ask my own."

"I liked the internet conferencing because I got to learn about two diseases that I didn't know a lot about and people brought up points on Cystic Fybrosis that I just took for granted."

Many of the students chose diseases to study because of relatives or friends' experiences, and this increased their interest, as these comments illustrate:

" I had great concern just because I have relatives that have the disease that I did [my research on], and it was interesting to know about it."

"I think this was a valuable experience, because I learned more about CF (the disease I choose). I had a friend that dies of complications of CF a few years ago, so it hit close to home. I know that a cure for CF is in the near future because of the research I have done."

This sort of personal interest was also evident in the Internet conferencing as illustrated by these questions: " My grandmother has Alzheimer's and I was wondering what kind of treatments are they coming out with in the near future. Is there any hope of a cure for her? Is it normal for her to have good days and bad days, sometimes she remembers me and sometimes she has no idea who I am, is that normal? Will she forget simple things like how to tie her shoes?"

Finally, a few students made some negative comments related to the amount of work this extra credit project entailed, e.g.,:

"I do think it was valuable although I do feel we spent a great amount of time on it for just being extra credit. I know our group honestly spent over 20 hours doing this project; that is more than I spent studying for all of the other exams combined!"

As a result of these comments, the instructor has decided to include this project as a regular part of his biology course, rather than as an extra credit option.

DISCUSSION

Assessment of computer simulations has typically focused on comparing such simulations with other kinds of learning environments or limiting assessment to questionnaires. Using a case-analysis task to measure understanding before and after this problem-based learning project, along with confidence measures, and in-depth interviews allowed us to understand more about the understanding and confidence students gain using problem based learning simulations such as Case It!. ? Based on students' surveys, interviews and open-ended comments, we found that their interest in particular biology concepts (e.g., DNA) increased and students were enabled to envision some of the social and ethical implications of DNA research in biotechnology.

The case analysis task measured transfer of learning but not depth of learning about specific diseases. Moreover, the data interpretation part of the case task was complex, in that it required an understanding of sex-linked mutations, and included both premutations as well as mutations. Additional research is needed to know why men in the experimental group scored better than women in the experimental group did on this part of the task. Both men and women in the experimental groups did show increased understanding of ethical issues related to genetic testing, however. Both groups became more confident of their understanding. Women may have gained knowledge about individual diseases not assessed by the case task, which was evident in their subjective feelings of understanding (confidence ratings) and in their interview responses.

This research corroborates previous research indicating that computer simulations motivate students (Blumenfeld, Soloway, Marx, Krajcik, Guzdial & Palincsar, 1991) in addition to enhancing scientific understanding (Amend & Tucker, 1989; Chambers,

Haselhuhn, Andre, Mayberry, Wellington, Krafka, Volmer & Berger, 1994), and providing students with experiments that might be otherwise unfeasible for introductory students (Stewart, Hafner, Johnson & Finkel, 1992). Students seemed particularly motivated by the connections they made between this problem-based case and their lives.

Finally, the value of problem posing and peer explanations in electronic and live poster discussions was illustrated by several student comments, by the additional research teams did in response to peer questions and by revisions to their Internet posters. Controversy and explanations produce greater gains in learning than interactions focused on lower levels of knowledge, such as definitions or facts (Lundeberg & Moch, 1995; Woloshyn, Pavio, & Pressley, 1992). Further research might analyze the kinds of comments students make to one another during Internet conferencing. Additional research is needed to understand more about the kinds of knowledge gained through Internet conferencing as compared to live poster conferences.

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Figure Caption

Figure 1. Southern blot for the sickle-cell anemia case.

Figure 2. Implications of Alzheimer's disease from webpage poster.

Figure 3. Changes in understanding ethical issues.

Figure 1. Southern Blot from Sickle-cell Anemia Case

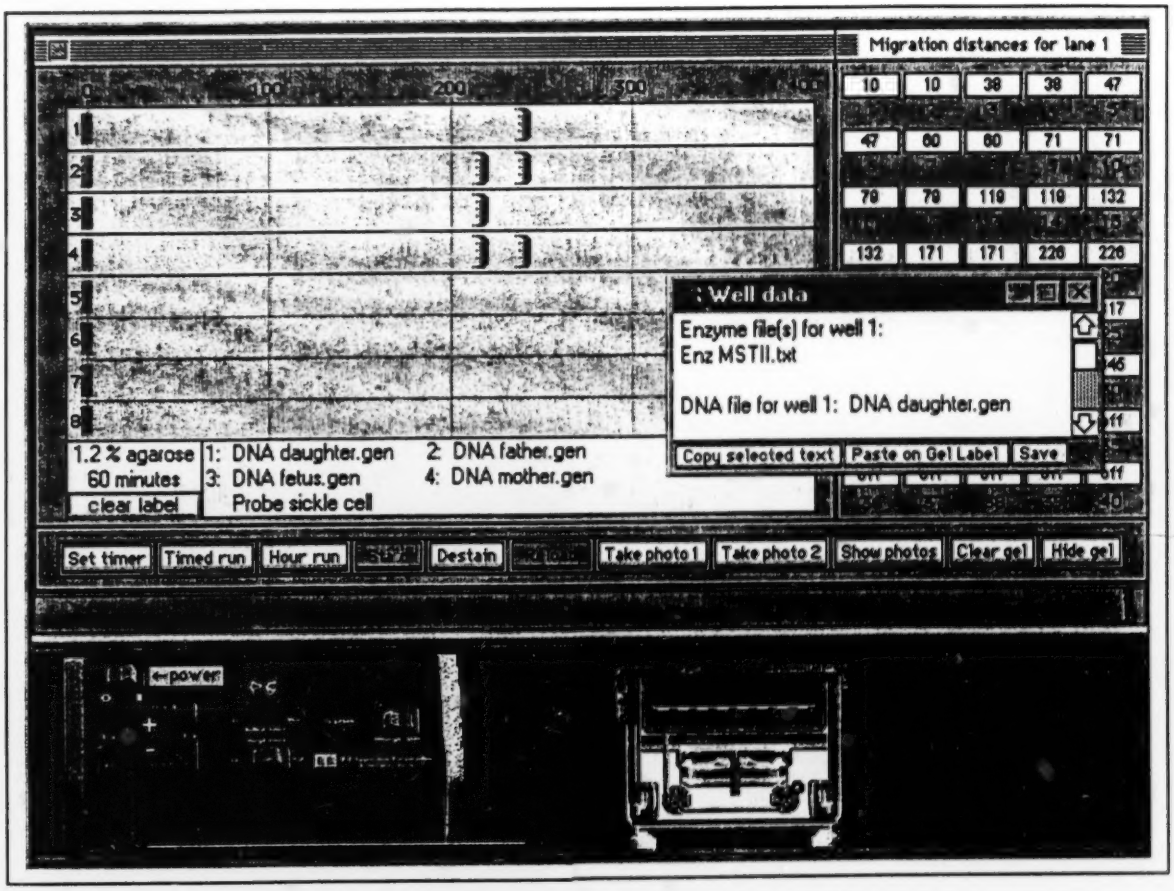

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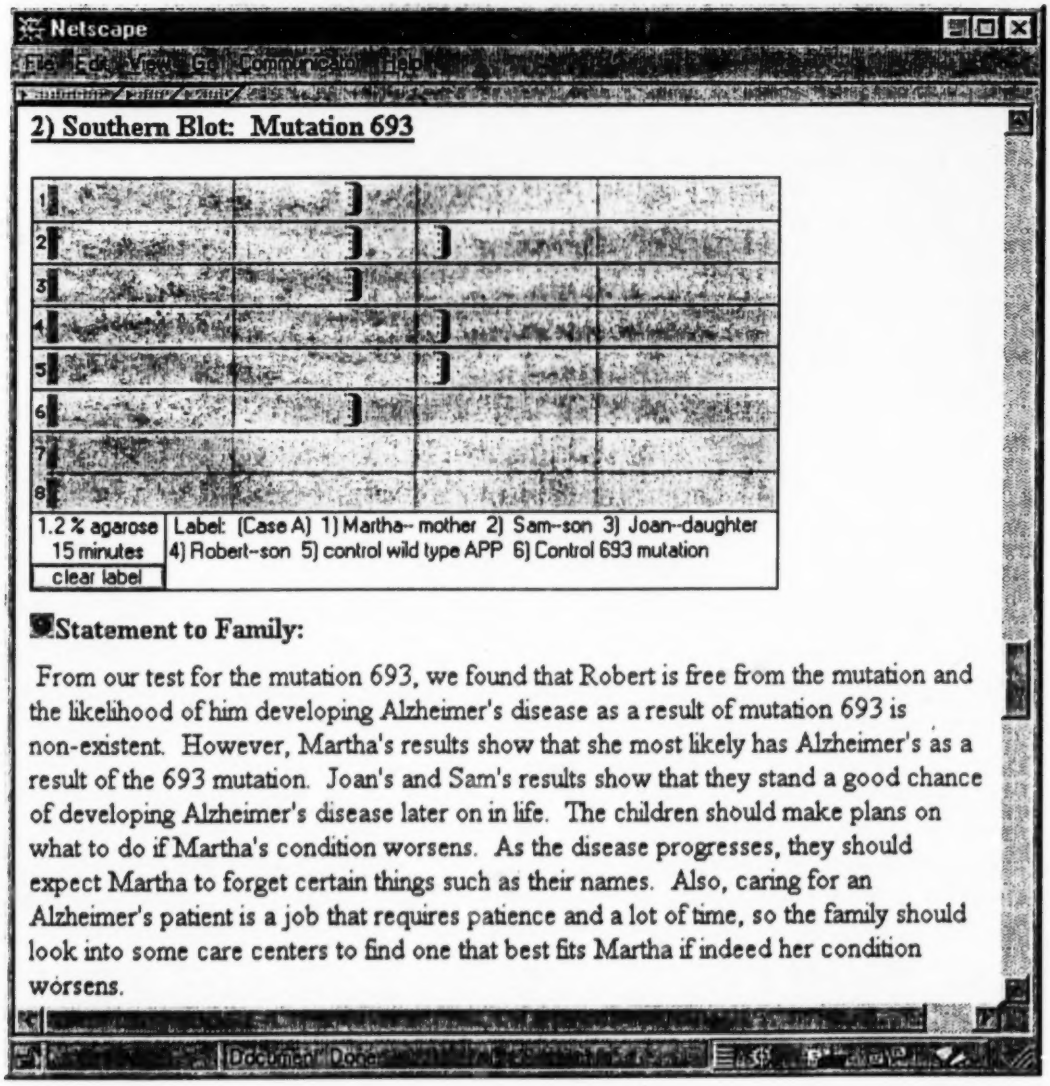
Figure 2. Portion of Student Poster Web Page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2) Southern Blot: Mutation 693
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6
7
8
1.2 % agarose
15 minutes
clear label
Label: (Case A) 1) Martha-- mother 2) Sam--son 3) Joan--daughter
4) Robert--son 5) control wild type APP 6) Control 693 mutation
Statement to Family:
From our test for the mutation 693, we found that Robert is free from the mutation and the likelihood of him developing Alzheimer's disease as a result of mutation 693 is non-existent. However, Martha's results show that she most likely has Alzheimer's as a result of the 693 mutation. Joan's and Sam's results show that they stand a good chance of developing Alzheimer's disease later on in life. The children should make plans on what to do if Martha's condition worsens. As the disease progresses, they should expect Martha to forget certain things such as their names. Also, caring for an Alzheimer's patient is a job that requires patience and a lot of time, so the family should look into some care centers to find one that best fits Martha if indeed her condition worsens.

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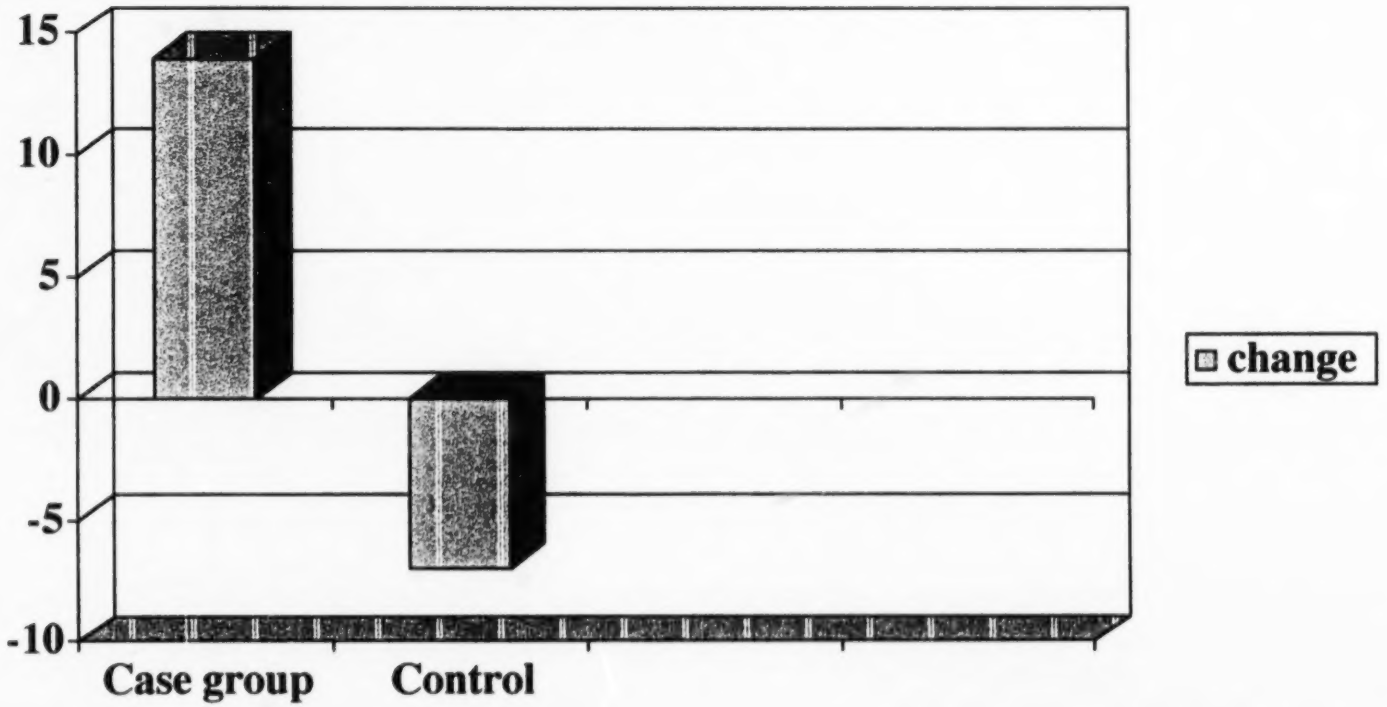
Figure 3

Changes in ethical understanding



Appendix A: Example of human genetics case: Alzheimer's disease

Appendix B: Survey of interest and confidence

Appendix C: Case analysis task

Appendix D: Scoring rubric used with case analysis task

Appendix A: Case 4. Alzheimer disease

Background: Alzheimer disease is by far the most common cause of dementia in aging persons. The disease symptoms are identical to other forms of senile dementia, and diagnosis had been possible only at autopsy by the detection of protein clusters called amyloid plaques in the cerebrum. The disease is multifactorial and inheritance patterns are complex. Some forms of familial Alzheimer disease appear to be inherited as autosomal dominant traits, while others are recessive. Spontaneous Alzheimer disease also can occur in the absence of inherited factors.

Mutations in at least four genes have been linked to Alzheimer disease. One of these is the amyloid precursor protein (APP) gene, which encodes the β-amyloid peptide found in the cerebral plaques of Alzheimer patients. The function of APP is not yet known, but certain APP point mutations are associated with inheritance of late-onset Alzheimer disease in some families. Two examples which can be detected by RFLP analysis are the codon 693 Glu to Gly mutation and the codon 717 Val to Ile mutation. The 693 mutation results in the loss of a MboII site, while the 717 mutation results in the gain of a BclI site.

The case: Martha, age 71, has been exhibiting increasingly severe symptoms of senile dementia and has been hospitalized for testing. She is in good health otherwise. Her three children - Sam (age 43), Joan (age 41) and Robert (age 38) - want to find out the cause of the dementia and determine the prognosis for Martha's future condition. They are also concerned that Martha may have a form of familial Alzheimer disease and want to know if they are at risk. The physician decides initially to test Martha for two mutations, 693 Gly and 717 Ile, in the amyloid precursor protein (APP) gene which are associated with inherited Alzheimer disease.

DNA samples:
Martha (mother)
Sam (son)
Joan (daughter)
Robert (son)
Control wild type APP
Control 693 mutation
Control 717 mutation

To test for the 693 Gly mutation, digest the DNA with MboII and perform a Southern blot using the APP probe. To test for the 717 Ile mutation, digest the DNA with BclI and then use the APP probe. Compare the test samples to the control samples, and use the results to determine the genotype of each individual. [Note: Small fragments are generated with the MboII digestion - use **1.2% agarose** and **short run times**.]

- Does Martha have either of these two APP mutations?
- Did any of Martha's children inherit an APP mutation?
- What conclusions can you draw regarding Martha's diagnosis?
- What can you tell Martha's children about their risk for Alzheimer disease?
- What issues are raised by this type of testing?

Appendix B: Survey of interest and confidence

Directions: If you have not yet had a lecture on this course material, you may think it inappropriate to say anything at all about your understanding of the topics below. However, completing this form will give us baseline data for describing any changes in confidence levels which may occur after lectures or other work.

Please indicate by checking the appropriate box, how confident you feel about your understanding of the concepts listed below.

Topic	no confidence	little confidence	some confidence	reasonably confident	very confident
Methods for detecting genetic diseases involving DNA					
DNA electrophoresis					
Interpretation of results from genetic tests					
Reasons for doing genetic testing					
Ethical issues involved in genetic testing					
How to locate current resources on diseases					

Please indicate by checking the appropriate box, how interested you are in each of the concepts listed below.

Topic	no interest	little interest	some interest	reasonably interested	very interested
Methods for detecting genetic diseases involving DNA					
DNA electrophoresis					
Interpretation of results from genetic tests					
Reasons for doing genetic testing					
Ethical issues involved in genetic testing					
How to locate current resources on diseases					

Appendix C: Case analysis task

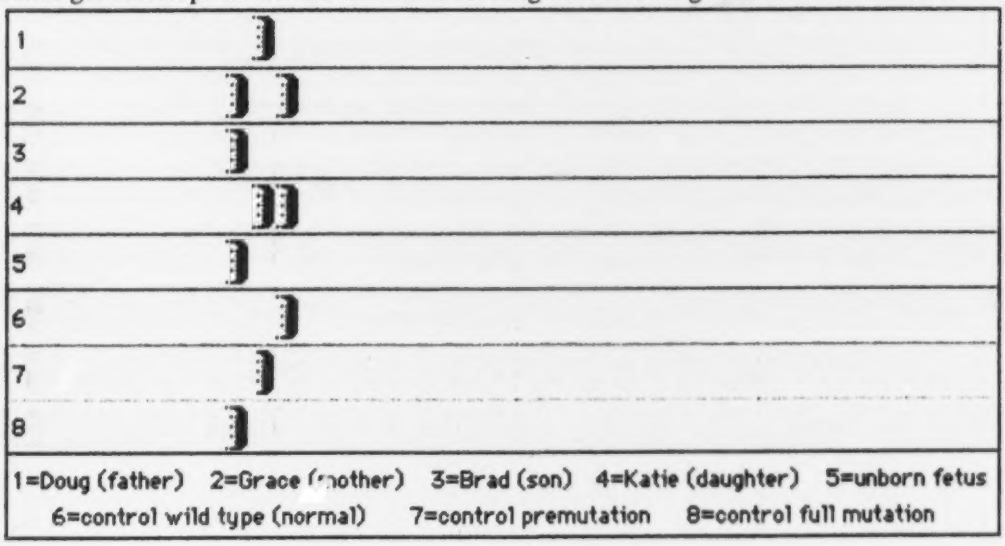
Please write short answers to the questions on the separate page. Your work will not affect your grade; we will aggregate your answers below to assess group understanding of the following concepts. After writing your answer, please indicate how confident you are that your answer is correct on a scale of 1-5, with 1 = uncertain and 5 = very confident.

Case history: Doug and Grace are expecting their third child. They suspect that their oldest child, Brad, might have Fragile X syndrome and decide to have the family undergo genetic counseling. Their daughter, Katie, shows no symptoms of Fragile X. They decide to undergo a test to determine the genotypes of all family members, including the unborn fetus.

Background: Fragile X syndrome, a sex-linked characteristic, is the leading cause of inherited mental retardation. The mutated gene that causes the disorder is called *fmr1* and is located on the long arm of the X-chromosome. It is currently unclear whether this trait is dominant or recessive, because both types of expression have been demonstrated.

The mutation involves exaggerated repetition of the CGG triplet in a portion of the *fmr1* gene near the 5' end. Those with a functional gene have 6 to 50 CGG repeats, whereas those with a full mutation have 200 or more such repeats. Between 50 and 200 repeats of the codon constitute a premutation. An individual with a premutation is considered a carrier, but does not display any symptoms of Fragile X. A premutation may undergo additional repetition to generate a full mutation.

After gel electrophoresis and Southern blotting the following results are obtained...



Name_____**Sex: ___M___F Major:**_____

1. **<u>As a genetics counsellor</u>, what would you advise this family about <u>ethical issues</u> raised by these results?**

Circle the letter that best reflects your confidence that your answer is correct.				
1	**2**	**3**	**4**	**5**
uncertain		mixed feelings	very confident	

2. **Based on your understanding of the molecular basis of the mutation, explain why the fragments in lanes 6, 7, and 8 are in different positions.**

Circle the letter that best reflects your confidence that your answer is correct.				
1	**2**	**3**	**4**	**5**
uncertain		mixed feelings	very confident	

Appendix D: Scoring rubric for open-ended responses on case analysis task

1) Advice to this family about ethical issues raised by these results.
This question was scored on a 0-3 scale:

<u>0 = no understanding of results:</u>

Example 1: "I would advise the family that their unborn child won't have the fragile x chromosome, but the uncertainty is always there if any more children are had, because the mother has, or could have a trace of fragile x in her genes."

Example 2: "A lot of family members seem to have a carrier to the symptoms."

1 = interpret results correctly and/or mention 1 ethical issue (e.g., abortion)

Example 1: "I would tell them that there is a good chance that the unborn baby will have fragile x syndrome. I would tell them that there are definitely options but wouldn't lean toward abortion."

2 = interpret results correctly and/or mention 2 ethical issues (or 1 ethical issue in depth)

Example 1: "The unborn fetus has the fragile x syndrome. Right now they have the choice of whether or not to have the baby, knowing that they already have one son with the syndrome. This also raises the question of whether or not to have more children knowing that they are both carriers of fragile x syndrome."

Example 2: "You would have to tell them that their baby is going to have fragile x syndrome thus they need to think about whether they can deal with another such child. If not, they may need to contemplate ending the pregnancy."

3 = interpret results correctly and/or mention 3 ethical issues (or 2 ethical issues in depth).

Example 1: "You should be aware that if you decide to have more children, there is a good chance that you could pass the genes for the disease on to them. You could choose to terminate this pregnancy, but you should also be aware that there are other options. You should do some more research on the disease before you make your decision. You could also keep the baby or give it up for adoption."

Total points possible = 3 Student's Score: _____

2) Based on your understanding of the molecular basis of the mutation, explain why the fragments in lanes 6,7, and 8 are in different positions.

Possible Concepts:	Point value	sts'points
Different lanes show different mutations or label lanes: 6-normal; 7=premutation; 8=full mutation.	1	_____
Repetitions (mutations) in DNA create larger fragments	2	_____
Larger fragments move more slowly through gel	2	_____
Enzyme cuts DNA into different sizes	1	_____
DNA has negative charge; fragments migrate to positive end	1	_____
Other meaningful explanation	1	_____

If students gives misinformation they get a 0

Total points possible = 8 Student's score: _____

Examples of a score of 0:

Example 1: "Because they each have different encoding it shows up differently on this type of graphing system."

Example 2: "It shows what is normal and what isn't normal."

Examples of a score of 1:

Example 1: "6 is the normal control group; 7 is the recessive trait; 8 is the full fragile x."

Example 2: "one is a normal control the other a premature form of the disease and the last is a positive position for fragile x."

Examples of a score of 2:

Example 1: "Lane 6 the blot is lighter and can pass through the gel easier than 7, 8."

Example 2: "Lane 6 is the control wild type (normal) and has 6 to 50 CGG repeats. Lane 7 is a control premutation and has between 50 and 200 repeats. Lane 8 is a control full mutation and has 200 or more repeats. The number of repeats affects the position of the fragments."

2) Based on your understanding of the molecular basis of the mutation, explain why the fragments in lanes 6,7, and 8 are in different positions.

Possible Concepts:	Point value	sts'points
Different lanes show different mutations or label lanes: 6-normal; 7=premutation; 8=full mutation.	1	_____
Repetitions (mutations) in DNA create larger fragments	2	_____
Larger fragments move more slowly through gel	2	_____
Enzyme cuts DNA into different sizes	1	_____
DNA has negative charge; fragments migrate to positive end	1	_____
Other meaningful explanation	1	_____

If students gives misinformation they get a 0

Total points possible = 8 Student's score: _____

Examples of a score of 0:

Example 1: "Because they each have different encoding it shows up differently on this type of graphing system."

Example 2: "It shows what is normal and what isn't normal."

Examples of a score of 1:

Example 1: "6 is the normal control group; 7 is the recessive trait; 8 is the full fragile x."

Example 2: "one is a normal control the other a premature form of the disease and the last is a positive position for fragile x."

Examples of a score of 2:

Example 1: "Lane 6 the blot is lighter and can pass through the gel easier than 7, 8."

Example 2: "Lane 6 is the control wild type (normal) and has 6 to 50 CGG repeats. Lane 7 is a control premutation and has between 50 and 200 repeats. Lane 8 is a control full mutation and has 200 or more repeats. The number of repeats affects the position of the fragments."